Wolbachia and Virus Protection in Insects

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Wolbachia pipientis are maternally transmitted, Gram-negative, obligate intracellular bacteria found in filarial nematodes, crustaceans, arachnids, and at least 20% of all insect species. Many *Wolbachia* bacteria increase their prevalence in populations by manipulating host reproductive systems (*1*). Insects are also commonly infected with viruses, and, considering the shared intracellular location, it is possible that *Wolbachia* may influence the outcome of virus infection in an insect host.

Drosophila melanogaster is commonly infected with *Wolbachia* and is a powerful model for studying host-pathogen interactions and antiviral responses (*2*). *Drosophila C virus* (DCV), a member of the *Dicistroviridae* family, is a natural pathogen of *D. melanogaster* and is found in 30 to 40% of both laboratory and wild-caught populations (*3*, *4*). Infection of adult *Drosophila* with DCV by injection can result in 100% mortality within 3 to 4 days. Although variation in susceptibility of fly strains to DCV-induced mortality has been recorded (*3*), the underlying basis for this variation has not been determined.

We compared the survival of flies infected with DCV in the presence or the absence of *Wolbachia* infection (Fig. 1 and fig. S1) (*5*). In flies from the standard laboratory strain, Oregon RC, *Wolbachia* infection delayed DCV-induced mortality compared with Oregon RC flies cured of *Wolbachia* infection (Fig. 1A). The delay in mortality corresponded with a delay in virus accumulation in *Wolbachia*-infected flies (fig. S2). The experiment was repeated with the fly strain w^{1118} with similar results observed (Fig. 1B). The survival curves of Oregon RC and w^{1118} *Wolbachia*-free flies were similar to those of two wild-type laboratory populations (Champetières and Oregon R) that are naturally uninfected with *Wolbachia* (compare Fig. 1, A and B, with fig. S1). Oregon RC and w^{1118} flies are infected with two closely related strains of *Wolbachia*, *w*MelCS and *w*MelPop, respectively (*6*). These results indicate that these strains of *Wolbachia*, in different genetic backgrounds of *Drosophila*, have an antiviral effect.

Two further viruses were tested with use of the survival bioassay: *cricket paralysis virus* (CrPV; *Dicistroviridae*), a natural *Drosophila* pathogen, and *Flock House virus* (FHV; *Nodaviridae*). The latter is unrelated to DCV and CrPV and is pathogenic in adult flies (*7*), although natural infections have not been reported. Like DCV, both CrPV and FHV induce rapid mortality when injected into adult *Drosophila*. All Oregon RC flies infected with *Wolbachia* and CrPV died within 17 days postinfection (Fig. 1C). In contrast, the *Wolbachia*-free Oregon RC flies died within 7 days of infection. Similarly, *Wolbachia*-free flies challenged with FHV died within 8 days of infection, whereas 26 days postinfection only 35% of the *Wolbachia*-infected flies had succumbed to FHV-induced mortality (Fig. 1D). These results indicate that the antiviral effect observed in *Wolbachia*-infected *Drosophila* functions to protect flies from diverse RNA viruses.

Typically *Wolbachia* manipulate host reproductive systems to increase the number of infected hosts within a population. However, *Wolbachia* strains that infect *D. melanogaster* do not induce these parasitic traits under field conditions at levels sufficient to invade host populations (*8*). Theory predicts that in the absence of strong reproductive parasitism *Wolbachia* should confer a fitness benefit to the host, but for *D. melanogaster* no such benefit has been identified in nature (*8*). Because both DCV and *Wolbachia* are common in wild *Drosophila* populations, the association of *Wolbachia* with a robust antiviral effect may confer a positive selective advantage to flies. If generalized, the antiviral protection associated with *Wolbachia* infection might be exploited in future strategies to reduce insect-transmitted diseases.

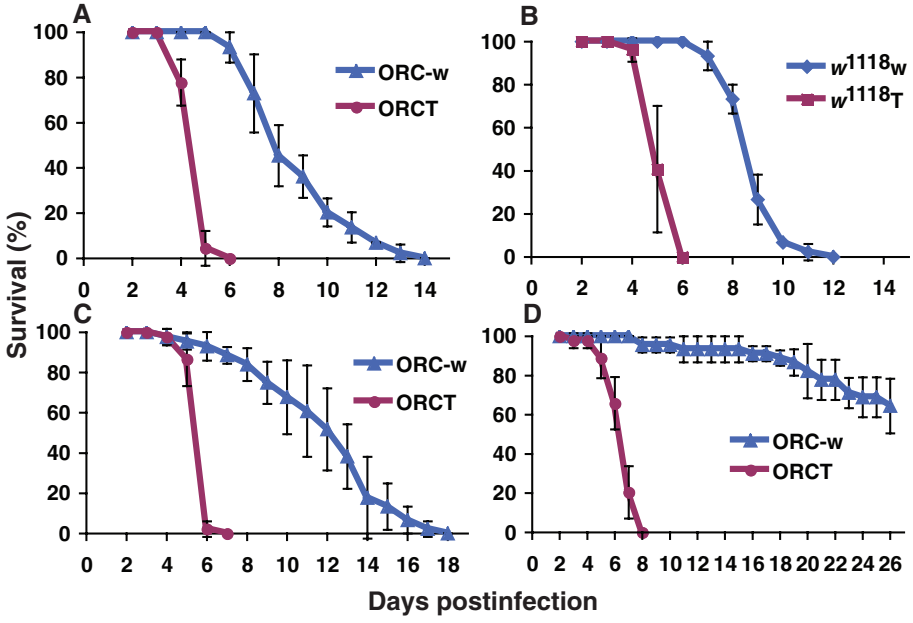

Fig. 1. Infection with *Wolbachia* protects flies from virus-induced mortality. The data shown represent the mean of triplicates, and the bars indicate standard error. The survival curves were significantly different for *Wolbachia* infected versus uninfected flies (Kaplan-Meier analysis, $P < 0.0001$ in each case). (**A**) Comparison of the survival of *Wolbachia*-infected (ORC-w) and uninfected Oregon RC (ORCT) flies after challenge with DCV. (**B**) Comparison of the survival of *Wolbachia*-infected (w) and uninfected (T) w^{1118} flies after challenge with DCV. (**C**) Comparison of the survival of *Wolbachia*-infected (ORC-w) and uninfected Oregon RC (ORCT) flies after challenge with CrPV. (**D**) Comparison of the survival of *Wolbachia*-infected (ORC-w) and uninfected Oregon RC (ORCT) flies after challenge with FHV.

References and Notes

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Supporting Online Material

www.sciencemag.org/cgi/content/full/322/5902/702/DC1
Materials and Methods
Figs. S1 and S2

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